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Article

Efficiencies of NF and RO Membranes on Pharmaceutical Removal and Membrane Fouling Effects

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Abstract. The efficiencies of nanofiltration (NF) and reverse osmosis (RO) membranes in removing carbamazepine (CBZ) and sulfamethoxazole (SMX) were studied. To do this, the NF and RO membranes NF-1 and RO-1 were used, and the isoelectric points of the NF-1 and RO-1 membranes were determined to be at approximate pH of 6.0. The NF-1 membrane's CBZ rejections at solution pH values of 5.0, 6.0, and 7.0 were in a slight range of 92-93%. Additionally, SMX rejections by the NF-1 membrane at the same three solution pH values were 87%, 91%, and 94%, respectively. Meanwhile, the RO-1 membrane's CBZ rejections at those solution pH values were also in a narrow range of 92-94%, and its SMX rejections were 94%, 97%, and 98%, respectively. Solution pH was found to have no effect on CBZ rejection but it did affect SMX rejection. Mixed pharmaceuticals showed insignificant change in rejections compared with those of single pharmaceutical. The effect of membrane fouling on SMX removal was observed. It was found that when the membranes were fouled by tannic acid (TA) in the presence and absence of calcium chloride (CaCl₂), the membrane's rejection of SMX was improved.

Keywords: Carbamazepine, membrane fouling, nanofiltration, reverse osmosis, sulfamethoxazole.

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1. Introduction

Pharmaceutical compounds, such as antibiotics, anti-inflammatory substances and antihistamines, have been used as a popular means for treating and preventing illnesses. Thus, abundant quantities of pharmaceuticals are produced and used for treating both humans and animals. However, some of the pharmaceutical compounds are discharged into the environment via wastewater treatment plants, expired products, veterinary pharmaceuticals, and excretion containing biotransformed pharmaceutical compounds [1]. Many researchers have studied the quantity of pharmaceutical compounds released from various sources. A water sample from Missouri was found to contain caffeine, ibuprofen and acetaminophen at concentrations of 224, 77.2, and 56 ng/L, respectively [2]. In surface water, metformin was found to range from 64 to 98 µg/L [3]. In addition, researchers have studied the drug concentrations in soil. It has been found that even the release of low levels of pharmaceutical compounds into the environment (ranging from levels of ng/L to µg/L) can have severe impacts on human health (e.g., renal lesions) and the environment (e.g., alterations of the gills on rainbow trout) [4] including the reproductive capacities of animals. Embryo production in adult zebras, for example, has been found to significantly decrease after they are exposed to pharmaceuticals [5].

Sulfamethoxazole (SMX) is a well-known sulfamide drug, which has been commonly used to treat various systemic infections in humans and animals since the early 1960s. To treat infections, SMX has been often used in combination with trimethoprim or pyrimethamine. It was found that the concentration of SMX in surface water ranged from 30 to 480 ng/L [6], and at a municipal sewage treatment plant, it was as high as 2000 ng/L [7-8]. Carbamazepine (CBZ) has been used to treat seizure disorders and neuropathic pain. The drug was first synthesized in the 1960s. CBZ has been found in surface water [9] and drinking water influent [7]. It has been widely detected in wastewater treatment plants, with concentrations as high as 3,800 ng/L [10].

Several methods have been applied in order to eliminate pharmaceuticals in the environment; however, there are many challenges associated with the effective removal of pharmaceutical compounds. A membrane is an advanced technological tool that is favored in the treatment of water because it is able to produce a higher quality of water. There are several types of membrane filtration methods; microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), reverse osmosis (RO), and the use of a membrane bioreactor [11-12] are well known methods. RO and NF membranes, in particular, can reject problematic compounds such as fluoride [13], have a small footprint, and are flexible for future application [14-15]. The rejection mechanisms of RO and NF membranes include size exclusion, electrostatic repulsion, and diffusion [16-18]. Nghiem and co-workers (2006) [19] studied the removal of SMX and CBZ from aqueous solutions using a loose NF membrane. They found that SMX and CBZ could be removed successfully. A problem associated with membrane filtration is membrane fouling. Membrane fouling is generated from the solute or particles that accumulate on the surface membrane or into the pores of the membrane [20]. Natural organic matter (NOM) is one of the foulants present in natural water sources. This phenomena affects the reduction of permeate flux and membrane degradation. However, some researchers have found that membrane fouling can have the positive effect of improving permeate quality [16, 21-22].

In this study, the factors (i.e., solution pH, single and mixed pharmaceutical compounds, and membrane fouling) affecting the efficiency of the NF and RO membranes for removing two specific types of pharmaceutical compounds, CBZ and SMX, were determined.

2. Materials and Methods

2.1. Pharmaceuticals

Two pharmaceutical compounds, namely carbamazepine (CBZ) (CAS no. 298-46-4) and sulfamethoxazole (SMX) (CAS no. 723-46-6), were selected. The physicochemical properties of the SMX and CBZ compounds are reported as follows. SMX is a derivative of the sulfanilamide class (MW 253.3 g/mol). SMX is composed of two aromatic rings linked with the SO₂NH₂ group. This functional group, which contains electrons from the drawing group, can develop a strong charge. Values of pK_{a1} and pK_{a2} are 1.6 and 5.7, respectively. CBZ is widely used antiepileptic drug (MW 236.3 g/mol). It is composed of two benzene rings combined with an azepine group that is connected to an amide group. A value of pK_a is 13.9.

2.2. Membranes and the Filtration Experiment

Two flat sheet polymeric membranes, namely, NF-1 and RO-1, were examined. NF-1 and RO-1 membranes are polyamide thin-film composite membranes. Salt rejections of NF-1 and RO-1 membranes were observed at 70% and 90%, respectively, under operating pressure 0.4 MPa and NaCl concentration 0.01 M. The properties of the NF-1 and RO-1 membranes, including their isoelectric points and pure water permeability were determined. A cross-flow unit (C10-T, Nitto Denko) was employed for the filtration experiments. The experimental set-up is shown in Fig. 1.

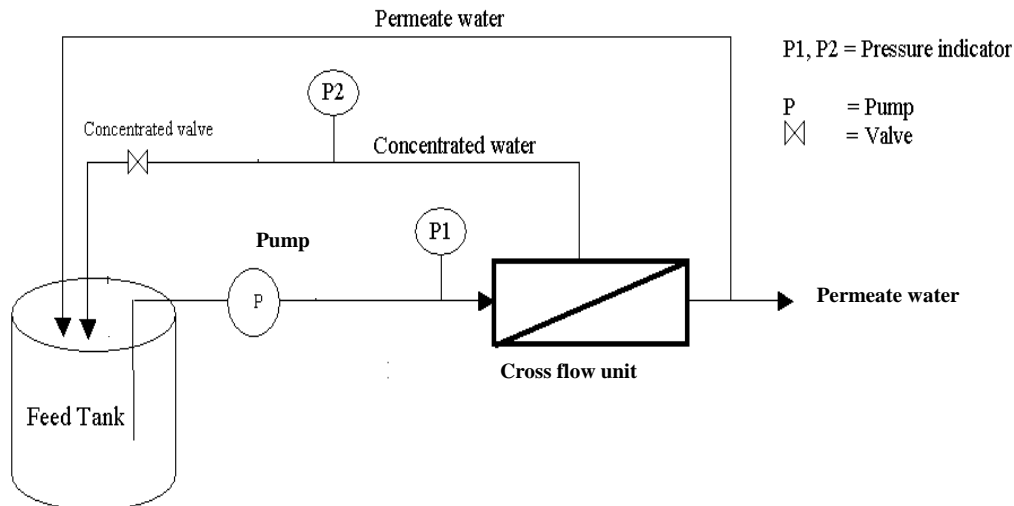


Fig. 1. Experimental set-up.

The method for determining the isoelectric point was adapted from the proposed procedures of Milonjić et al. (1975) and Babić et al. (1999) [23-24]. In addition, the method was previously applied to determine the isoelectric point of a dolomite sorbent for fluoride adsorption [25]. Membrane sheets were cut small in size (4x3 cm). A NaCl solution (0.01 M) was prepared. Hydrochloric acid (HCl) and sodium hydroxide (NaOH) (0.01 mol/L) were used to adjust the pH of the sodium chloride (NaCl) solution to a pH range of 2-10. The sheets of the membranes were immersed in each volumetric bottle that contained the pH adjusted solution. Then, all the volumetric bottles were shaken for 24 hours at 100 rpm at room temperature. Afterwards, the pH of each bottle was measured again. The initial and final pH values were taken to plot the graph. The isoelectric point was obtained from the common plateau of the plot.

Pure water permeability was examined as follows. One liter of pure water was filtered through the cross-flow unit at three different operating pressures, 0.2, 0.3, and 0.4 MPa, under a controlled temperature of 30 ± 2 °C. Permeate water was collected every ten minutes (10, 20, and 30 minutes) for the initial half hour. After the initial half hour, the permeate water was collected in intervals of 60 minutes (60, 120, 180, and 240 minutes) up until the fourth hour, to confirm the steady state permeate flux.

2.3. Removal of CBZ and SMX by the Membranes

Both single and mixed pharmaceutical solutions were examined. For a single pharmaceutical solution, a 5 mg/L concentration of each pharmaceutical was prepared. For a mixed pharmaceutical solution, the concentration of mixed solution was the same as single solution about 5 mg/L of each. The solution pH values were adjusted using HCl and NaOH to three levels: (1) a pH level below the isoelectric point, (2) the pH level at the isoelectric point, and (3) a pH level above the isoelectric point. The solutions were filtered through the membranes at 0.4 MPa under a controlled temperature of 30 ± 2 °C. The experiment was performed in recycle mode; thus, the permeate water and concentrated water were returned to the feed tank. When the permeate flux reached a steady state, the permeate water was collected. Then, the CBZ and SMX concentrations in the feed water, concentrated water, and permeate water were measured by a reverse phase high performance liquid chromatography (HPLC) (Varian, Prostar, USA) with the C-18 column (ZORBAX Eclipse XDB-C18 2.1x100 mm (3.5 μ m), Agilent, USA). An UV-Vis detector was used to measure the

concentrated, feed and permeate water of CBZ and SMZ. The detection of wavelengths of 280 nm was recorded for CBZ and SMX. CBZ and SMX rejections (%) were computed as follows:

$$\text{Rejection (\%)} = \left[1 - \frac{C_p}{C_f} \right] \times 100 \quad (1)$$

where C_p is the pharmaceutical concentration of the permeate water and C_f is the pharmaceutical concentration of the feed water.

2.4. Influence of Membrane Fouling on SMX Removal

The influence of tannic acid (TA) on SMX removal was further studied. TA is a soluble resistant polyphenolic compound, which is normally found in natural surface water. Molecular weight distribution of TA is in the range of major dissolved organic matters (DOMs) in the natural surface water [26-28]. Hence, a membrane fouling via TA during a membrane treatment process is considered. A 5 mg/L concentration of SMX was prepared. Then 10 mg/L concentrations of TA were prepared in the presence and absence of 0.001 M calcium chloride (CaCl_2). The solution pH was 7.0. The solutions were filtered through the membranes at 0.4 MPa under a controlled temperature of 30 ± 2 °C. One liter of feed solution was filtered through the cross-flow unit until a water flux decline was observed. Then, the concentrated, feed, and permeate waters were collected to measure their SMX concentrations with HPLC and their dissolved organic carbon (DOC) concentrations using a TOC analyzer (TOC vcpH, Shimadzu, Japan).

In addition, obtained results were further interpreted by using statistical software. The statistical software was used for statistical analyses of CBZ and SMX rejection by NF-1 and RO-1 membranes, membrane fouling effects on permeate water flux and SMX removal.

3. Results

3.1. Isoelectric Point

NF-1 and RO-1 membranes are composite membranes. They have polyamide (PA) active layers that contain two functional groups: a carboxylic group ($-\text{COOH}$) and an amine group ($-\text{NH}_2$). The carboxyl group ($-\text{COOH}$) in a solution with basic pH dissociates and becomes negatively charged ($-\text{COO}^-$), whereas the amine group, the protonated amino group ($-\text{NH}_3^+$) in an acidic pH solution becomes positively charged [29-30]. The isoelectric point observation results are shown in Fig. 2 and Fig. 3.

The NF-1 and RO-1 membranes are polymeric membranes, containing two layers; an active layer and a supporting layer. The active layer controls the separation mechanisms of the membranes, whereas the supporting layer maintains the strength of the membranes. The isoelectric points of the active layers on the NF-1 and RO-1 membranes were observed at approximate pH of 6.0, which means they had neutral or nearly zero surface charges. When a solution pH was higher than the pH at the isoelectric point, the membrane surface became negatively charged because protons from the carboxylic group on the membrane surface deprotonated into the solution. When a solution pH was lower than the pH at the isoelectric point, the membrane surface became positively charged due to protons from the solution protonated into the amine group on the membrane surface.

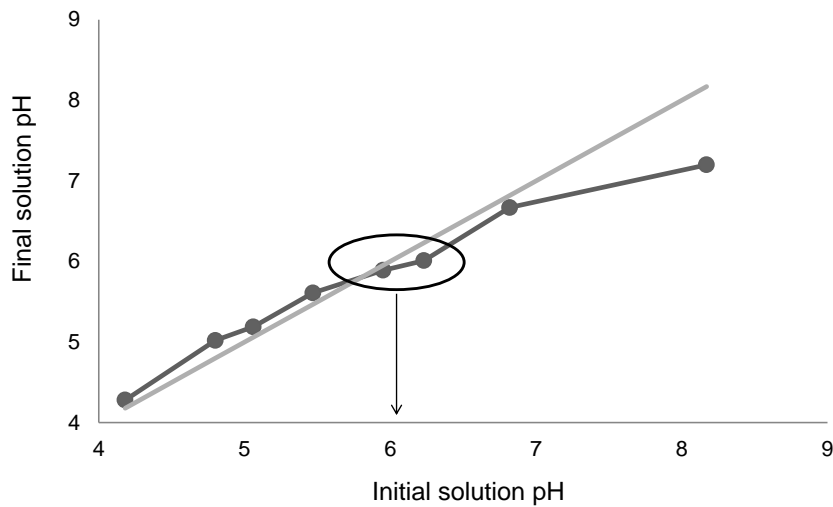


Fig. 2. Isoelectric point determination of the NF-1 membrane.

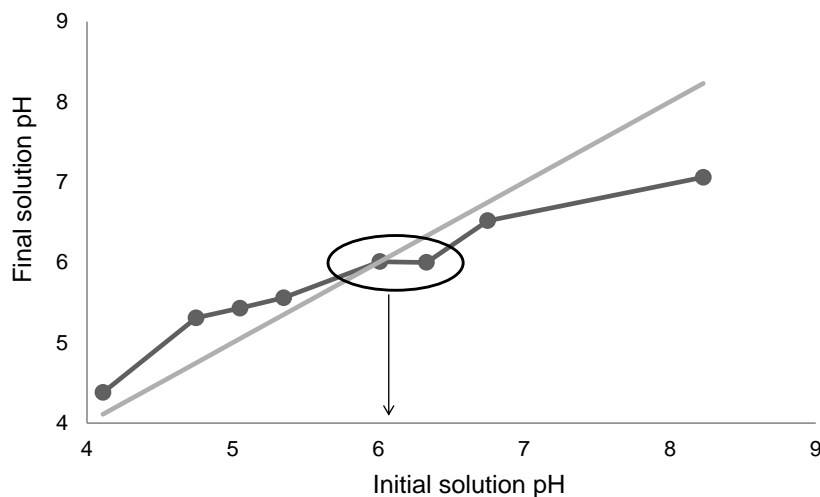


Fig. 3. Isoelectric point determination of the RO-1 membrane.

3.2. Pure Water Permeability

At the operating transmembrane pressures of 0.165, 0.275, and 0.375 MPa, the permeate water fluxes of the NF-1 membrane were 0.48, 0.96, and 1.46 $\text{m}^3/(\text{m}^2\cdot\text{day})$, respectively. Meanwhile, those obtained from the RO-1 membrane were 0.18, 0.36, and 0.48 $\text{m}^3/(\text{m}^2\cdot\text{day})$, respectively, under the same operating transmembrane pressures. Figure 4 shows the permeate water flux at the steady state of each operating transmembrane pressure for the NF-1 and RO-1 membranes, respectively. The slopes between the permeate water flux and operating transmembrane pressure (TMP) indicate the pure water permeability (K_w) of the membrane as follows;

$$\text{Permeate water flux} = K_w \times \text{TMP} \quad (2)$$

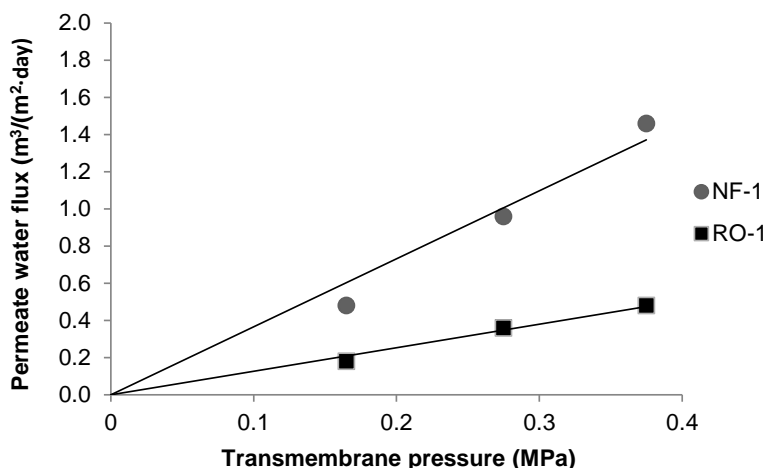


Fig. 4. Permeate water flux of each operating transmembrane pressure of the NF-1 and RO-1 membranes.

As shown in Equation (2) and Fig. 4, the pure water permeabilities (K_w) of NF-1 and RO-1 membranes were 3.66 and 1.27 $\text{m}^3/(\text{m}^2 \cdot \text{day} \cdot \text{MPa})$, respectively. Thus, NF-1 membrane gave higher pure water permeability than that of the RO-1 membrane, indicating the larger pore size of the NF-1 membrane. Dolar and co-workers (2011) reported the pore diameter of the NF-1 membrane to be 1.36-1.92 nm [31], which classified it as a NF membrane. The pore diameter of the RO-1 membrane was approximately 0.6-0.75 nm, which classified it as a RO membrane. Therefore, the results could indicate that a higher quantity of permeate water passed through the larger pore size membrane than the smaller pore size membrane. In addition, the larger pore size of the NF-1 membrane also suggested that its removal efficiency could be less than that of the RO-1 membrane.

3.3. Pharmaceutical Removal

The results of the previous section showed that the isoelectric points of the NF-1 and RO-1 membranes were identified at pH 6.0. Hence, the pH of the CBZ and SMX solutions were adjusted to pH 5.0, 6.0, and 7.0, respectively. The removal results of CBZ and SMX by the NF-1 and RO-1 membranes are reported as shown in Tables 1 and 2. CBZ rejection percentages by the NF-1 membrane at solution pH values of 5.0, 6.0, and 7.0 were observed in a slight range of 92-93%. Additionally, SMX rejection by the NF-1 membrane at solution pH values of 5.0, 6.0, and 7.0 were 87%, 91%, and 94%, respectively. With regard to the RO-1 membrane's results, CBZ rejection percentages at the same three solution pH variations were in a range of 92-94% whereas SMX rejection percentages were 94%, 97%, and 98%, respectively.

From statistical analyses, the effects of solution pH and membrane type on CBZ and SMX removals by NF-1 and RO-1 membranes were not significantly different (at $p < 0.05$). However, the removals of SMX by NF-1 and RO-1 membranes showed a positive correlation when solution pH increased.

Table 1. Removal of CBZ and SMX by the NF-1 membrane.

| Pharmaceutical | Feed solution pH | Percent removal |
|----------------|------------------|-----------------|
| SMX | 5.0 | 87 |
| | 5.9 | 91 |
| | 7.1 | 94 |
| CBZ | 5.0 | 93 |
| | 6.1 | 93 |
| | 7.1 | 92 |

Table 2. Removal of CBZ and SMX by the RO-1 membrane.

| Pharmaceutical | Feed solution pH | Percent removal |
|----------------|------------------|-----------------|
| SMX | 5.0 | 94 |
| | 6.1 | 97 |
| | 7.1 | 98 |
| CBZ | 5.1 | 93 |
| | 6.1 | 94 |
| | 6.9 | 92 |

From the results of pharmaceutical removal, the pK_a value of CBZ was 13.9; therefore, CBZ had no effect on the charge of the CBZ molecule when the solution pH was in the range of 5.0 to 7.0. In contrast, SMX's pK_{a1} value was 1.8 and its pK_{a2} value was 5.6. This meant that the SMX molecule could turn into a negatively charged molecule when the solution pH was higher than its pK_{a2} value. The rejection of CBZ was relatively independent of pH, whereas the rejection of SMZ was relatively pH dependent [19,32]. Hence, the removal of CBZ could be controlled by size exclusion and diffusion mechanisms, while the removal of SMX could be controlled by size exclusion, diffusion, and electrostatic repulsion mechanisms when the solution pH was in the 5.0-7.0 range.

In addition, the hydrophobicity properties of CBZ and SMX might affect the removal efficiencies of RO-1 and NF-1 membranes. Hydrophobicity was represented by octanol-water partition coefficient ($\log K_{ow}$). The $\log K_{ow}$ values of CBZ and SMX were 2.45 and 0.89, respectively. Accordingly, both of them were categorized as hydrophilic compounds. The hydrogen bonds between pharmaceuticals and water molecules might be influenced by water-water bonding because of the polar groups. Therefore, the pharmaceutical compounds with water molecules can change in diameter; this finding was confirmed by Braeken and co-workers in 2005 [33]. They found that the molecules of xylose increased from 0.69 to 1.21 nm when formed the H-bond. As a result, pharmaceuticals with high hydrophilic properties (e.g., CBZ and SMX) can find difficulty when passing through membranes.

The rejection results of CBZ by the RO-1 membrane were not different compared with those obtained from the NF-1 membrane. Nevertheless, the RO-1 membrane showed a higher removal efficiency of SMX than another membrane. It could have been due to the smaller pore size of the RO-1 membrane and the larger charge density on the RO-1 membrane, which relates to the mentioned removal mechanisms.

Furthermore, there was not much change in removal percentages for the mixed pharmaceuticals comparing with the single pharmaceuticals, as can be seen in Table 3. It was supported by a statistical analysis, which found that the removals of mixed and single pharmaceuticals by NF-1 and RO-1 membranes were not significantly different (at $p < 0.05$).

Table 3. Removal of the mixed CBZ and SMX solution by the NF-1 and RO-1 membranes.

| Membrane | Feed solution pH | Mixed Pharmaceuticals | Percent removal |
|----------|------------------|-----------------------|-----------------|
| NF-1 | 7.2 | CBZ | 91 |
| | | SMX | 94 |
| RO-1 | 7.1 | CBZ | 99 |
| | | SMX | 99 |

3.4. Fouling Effects on SMX Removal

The SMX removal percentages of the fouled RO-1 membrane in the presence and absence of $CaCl_2$ were both 99%. With regard to the fouled NF-1 membrane, its SMX removal percentages in the presence and absence of $CaCl_2$ were 98% and 99%, respectively. The results are shown in Table 4.

From a statistical analysis, the effects of membrane fouling on SMX removals by NF-1 and RO-1 membranes were not significantly different (at $p < 0.05$). However, the removals of SMX by NF-1 and RO-1 membranes were found to be improved when the membranes were fouled with tannic acid (TA) in the presence and absence of $CaCl_2$, especially in the NF-1 membrane case.

Table 4. Removal of SMX by fouled membranes.

| Condition | Fouled membrane with | | Virgin membrane |
|-----------|----------------------------|--------|-----------------|
| | Tannic + CaCl ₂ | Tannic | |
| NF-1 | 98 | 99 | 94 |
| RO-1 | 99 | 99 | 98 |

In case of fouling effects on SMX removal, tannic acid might have accumulated and formed a densely fouled layer on the membrane surface. The densely fouled layer could have acted as another filtration layer, which increased the membrane's SMX removal. Another possibility could be due to an interaction between SMX and tannic acid. Other researchers have studied the effects of inorganic salt (CaCl₂) on pharmaceutical removal. It was found that calcium ions (Ca²⁺) reduced the Donnan potential length between surface membranes and pharmaceuticals, decreasing the rejection of pharmaceuticals [34-35]. In this study, when the membrane was fouled with TA, the presence of CaCl₂ did not affect the densely fouled layer. Furthermore, an increased removal of SMX was observed. It could be stated that a low concentration of calcium ions (less than 6 mg/L) does not affect the formation of the densely fouled layer [31].

Additionally, Figs. 5-8 show normalized fluxes of the NF-1 and RO-1 membranes during the filtration experiment. The normalized flux was determined by dividing a permeate water flux (J) with a pure water flux (J_0). Pure water was pressurized and filtered through the cross-flow unit for the first hour. Then, the SMX solutions containing TA with and without CaCl₂ were further filtered through the cross-flow unit. Since experimental set-up indicated the recycle of permeate and concentrated line, this corresponded to the result which the permeate water flux gave relatively constant during filtration.

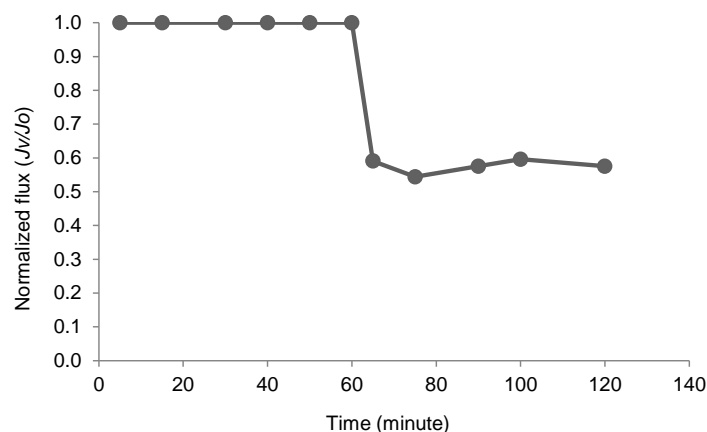
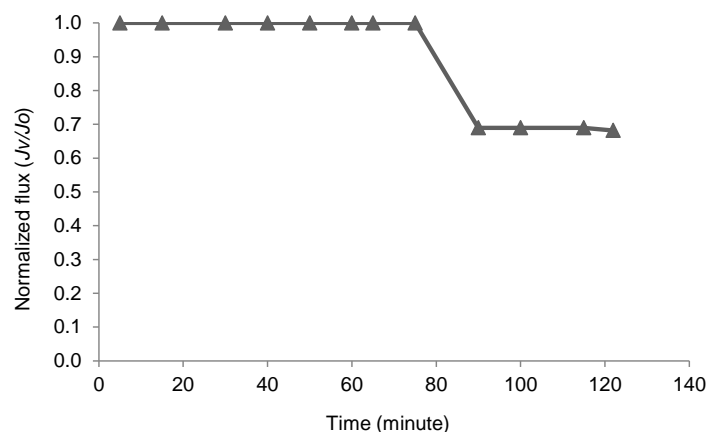
Fig. 5. Normalized flux of the NF-1 membrane from the SMX solution in the presence of TA and CaCl₂.

Fig. 6. Normalized flux of the NF-1 membrane from the SMX solution in the sole presence of TA.

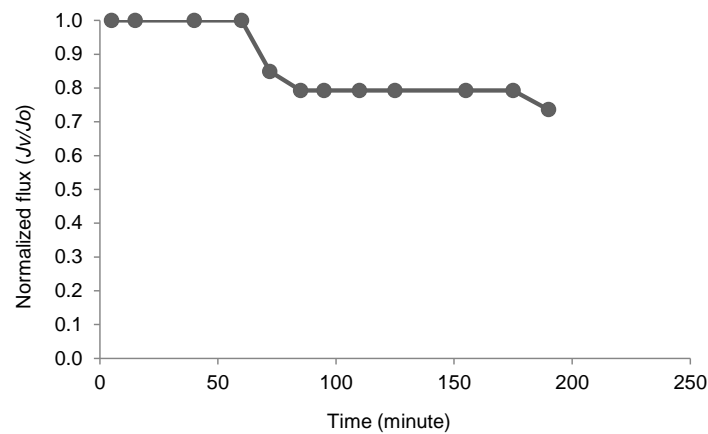


Fig. 7. Normalized flux of the RO-1 membrane from the SMX solution in the presence of TA and CaCl₂.

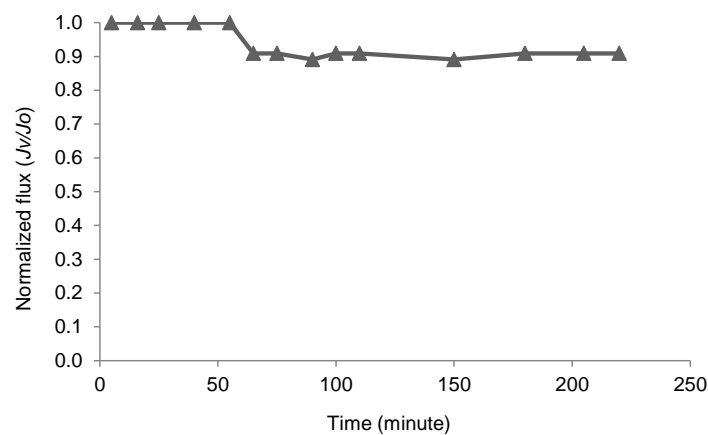


Fig. 8. Normalized flux of the RO-1 membrane from the SMX solution in the sole presence of TA.

The results showed that permeate water flux declined due to membrane fouling when the SMX solution containing TA in the presence and absence of CaCl₂ was further filtered through the cross-flow unit. In case of NF-1 membrane, the permeate water fluxes decreasing due to membrane fouling with TA in the presence and absence of CaCl₂ were observed at 42% and 31%, respectively. In case of RO-1 membrane, the permeate water fluxes decreasing due to membrane fouling with TA in the presence and absence of CaCl₂ were observed at 23% and 9%, respectively. Membrane fouling with TA in the presence of CaCl₂ was severer than that of the absence of CaCl₂. This indicated that the permeate water flux of the SMX solution containing TA in the presence of CaCl₂ was worse than the flux obtained in the absence of CaCl₂. The presence of calcium in the synthetic wastewater accelerated membrane fouling; therefore, the flux declined dramatically, which was consistent with the findings of other studies [34, 36]. Hoek and Elimelech (2003) found that a membrane fouled by humic acid and CaCl₂ might cause a severe flux decline [37]. The initial rapid fouling was due to pore blocking and then the fouling was due to the cake layer formation. Multivalent cations such as calcium perform as bridging reagents between carboxylic and phenolic functional groups of organic foulants, and it is the bridging reagent that forms the cross-linked fouling layer [38]. Furthermore, a severer decline in the permeate water flux of the NF-1 membrane was observed. This could have been due to pore blocking by tannic molecules on the membrane's surface [39].

4. Conclusion

This study applied NF-1 and RO-1 membranes for CBZ and SMX removal. Both the NF-1 and RO-1 membranes provided high removal efficiencies. The removal of CBZ was relatively independent of pH, whereas the removal of SMX was relatively pH dependent. Consequently, the removal of CBZ could be controlled by size exclusion and diffusion mechanisms, and the mechanisms for controlling SMX removal could be size exclusion, diffusion, and electrostatic repulsion. The membranes showed insignificant removal of mixed pharmaceuticals comparing with the single pharmaceutical. When the membranes were fouled by tannic acid, a dense fouled layer on the membrane surface could be formed in the presence and absence of CaCl₂, this consequently increased SMX removal.

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